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EXPOSURE OF CHILDREN WITH CYSTIC FIBROSIS TO ENVIRONMENTAL TOBACCO SMOKE

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Abstract *Background.* In children, passive exposure to environmental tobacco smoke has been associated with growth suppression and an increased frequency of respiratory tract infections. On the assumption that this association would be more pronounced in children with chronic pulmonary disease, we examined the growth, nutritional status, lung function, and clinical condition of children with cystic fibrosis in relation to their exposure to environmental tobacco smoke.

Methods. We studied 43 children (age, 6 to 11 years) on entry to a summer camp and then again after two weeks in this smoke-free environment. Twenty-four of the children (56 percent) came from homes with smokers.

Results. There appeared to be a dose-dependent relation between the estimate of smoke exposure (cigarettes smoked per day in the home) and overall severity of disease, as assessed by the age-adjusted rate of hospital admissions ($r = 0.58$), peak expiratory flow rate ($r = -0.38$), and measures of growth and nutrition, including weight percentile ($r = -0.37$), height percentile ($r = -0.34$), midarm circumference ($r = -0.42$), and triceps skin-fold thickness ($r = -0.34$). These effects were most evident in the girls. When only the 24 children from homes with smokers were analyzed, however, the dose-dependent relation was present only for the number of hospital admissions and for height. Among the children with good lung function (n = 21) or with normal weight for height (n = 27) at the start of camp, those who had been exposed to tobacco smoke gained significantly more weight during the two weeks of camp than did the children from smoke-free homes.

Conclusions. These data suggest that passive exposure to tobacco smoke adversely affects the growth and health of children with cystic fibrosis, although the possibility cannot be ruled out that social, economic, or other factors determined both the smoking status of the household and the nutritional status of the children. (N Engl J Med 1990; 323:782-8.)

EXPOSURE to environmental tobacco smoke has been postulated to have an adverse effect on lung function[1-4] and growth[5-11] in normal children. There is a dose-dependent relation in the frequency of respiratory tract infections in infants and young children exposed to tobacco smoke.[1-3] Some studies have shown a statistically significant decline in pulmonary function in healthy children exposed to tobacco smoke,[12] and there is a suggestion that children with asthma have more frequent attacks and more severe disease when exposed to environmental tobacco smoke.[3] There is also a body of evidence relating growth retardation and weight reduction to active smoking in adults[13,14] as well as to passive smoking in children[7-11]; a similar relation has been found in infants born to mothers who smoke[5-7] and in infants born to mothers passively exposed to tobacco smoke.[15]

Cystic fibrosis is an autosomal recessive disease whose major manifestations are recurrent and chronic pulmonary infections and pancreatic malabsorption

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with growth retardation.[16,17] Children with this disease may therefore be at increased risk for harm from exposure to tobacco smoke. We studied the relation between exposure to smoke and clinical status, growth and nutrition, and pulmonary function in a group of children between the ages of 6 and 11 years attending a summer camp for children with cystic fibrosis. The camp setting was ideal for collecting information about the children's medical history and exposure to tobacco smoke. Furthermore, this setting facilitated the organized collection of data on growth, nutrition, and pulmonary function on entry into camp and the assessment of changes in these measurements after two weeks of a balanced, high-quality diet, carefully administered medications, and physiotherapy in an environment free of tobacco smoke.

Methods

At the start of the two-week summer camp for patients with cystic fibrosis (Camp Merrywood in eastern Ontario), a medical history was obtained for each camper as part of the registration process, and all had a physical examination, which included the measurement of height, weight, and routine vital signs. After informed consent was obtained from the parents or guardians of the campers, a group of physicians, nurses, and medical students from Queen's University (Kingston, Ont.) and the University of Ottawa cystic fibrosis centers collected additional data on 43 of the 46 campers as detailed below. Incomplete data were collected for one boy who left early (for family reasons) and another who arrived a day late. One of the campers declined participation in the study. This study was approved by the March of Dimes, which coordinates Camp Merrywood, by the administrators of the camp, and by the Queen's University Human Research Committee.

The medical history was supplemented by a questionnaire that was completed by the parents. Data were collected about the severity of the camper's illness (e.g., frequency of cough, amount of sputum, and number of hospital admissions) and about his or her home, including a listing of all household members, their ages, health status (including recent respiratory tract infections), and tobacco consumption, expressed as the number of cigarettes smoked per day in the home. These data were checked for accuracy by reviewing the questionnaire both with the parent who completed the form and with the child. Historical data were further verified by cooperating Ontario cystic fibrosis centers after camp was completed.

In each participating child, midarm circumference and triceps skin-fold thickness were measured (skin-fold spring-loaded caliper, John Bull British Indicators),[18] and pulmonary function was evaluated (Vanguard spirometer and recorder, Life Support and Equipment). Clinical progress was assessed with the Shwachman–Kulczycki system,[16] which uses historical data and physical-examination results to calculate a score for the general, nutritional, and physical health of patients with cystic fibrosis. All the children were familiar with pulmonary-function testing procedures. Spirometry was repeated until three acceptable curves were produced for each child,[19] from which forced vital capacity (FVC), forced expiratory volume in one second, peak expiratory flow rate (PEFR), and expiratory flow rate measured between 25 percent and 75 percent of the forced vital capacity were recorded from the curve in which the total of FVC and forced expiratory volume in one second was largest. Pulmonary-function data were analyzed after camp by computer and expressed both in terms of absolute volumes and flow rates and as the percentages of the predicted values for Ontario children of the same height and sex.[19] The physical examination, spirometry, and anthropomorphic measurements were repeated on the last day of camp. The investigators who conducted the physical examinations, evaluated pulmonary function, and collected nutritional data were unaware of the details of the medical history — specifically, the children's exposure to tobacco smoke.

Statistical analysis was performed with the StatView 512+ statistics package (Abacus Concepts) and a Macintosh II computer (Apple Computer) and reviewed by a statistician. Comparisons between children who were exposed to environmental tobacco smoke and those who were not were made with an unpaired t-test. Changes in pulmonary function and nutritional status in the two groups of children while they were at camp were analyzed with an unweighted, two-tailed, paired t-test. Analysis of variance was used to investigate the interaction between exposure to environmental tobacco smoke and growth. Results are presented as means ±SD. All P values of less than 0.05 were considered to indicate significance.

One severely ill child required constant nasal administration of oxygen and was unable to participate in camp activities. Because this girl spent most of the camp session in the infirmary, initial data related to her growth and health were recorded, but she was excluded from analyses dealing with changes noted after camp.

Results

Patient Population and Severity of Illness

The children were 72 to 143 months of age (mean, 108.9±16.7) and had been seen at one or more of the seven cystic fibrosis centers in Ontario. There were 18 girls and 25 boys in the group that completed the study. Twenty-four of the children (56 percent) came from households with smokers (24.4±14 cigarettes smoked in the home per day), and nearly 40 percent had mothers who smoked (18.6±9.2 cigarettes per day). None of the children actively smoked.

Clinical scores indicated that as a group these children were in fairly good health. Of a possible total of 25 points, the Shwachman–Kulczycki general score for the group was 23.2±3.1, the physical score was 22.0±4.3, and the nutrition score was 22.1±4.0. There was a correlation between the total score and the number of cigarettes smoked in the home ($r = -0.34$, $P = 0.03$), but this was accounted for almost entirely by the strong correlation between the nutrition subscore and exposure to environmental tobacco smoke ($r = -0.41$, $P = 0.006$).

Because the total number of hospitalizations increases with the age of the patient, one measure of illness severity is the normalized hospital-admission rate, obtained by dividing the total number of admissions by the child's age in months. Normalization of the admission rate minimizes the effect of the broad age range of the children and more accurately reflects the severity of illness. In the group as a whole, the normalized hospital-admission rate was strongly related to the number of cigarettes smoked in the home ($r = 0.58$, $P<0.0001$) (Fig. 1). Examining data from just the 24 children exposed to tobacco smoke still yielded a significant, dose-dependent relation ($r = 0.55$, $P<0.01$). There was a significant correlation of exposure to tobacco smoke with the normalized hospital-admission rate for the girls ($P = 0.0005$), and analysis of variance suggested that this factor alone accounted for 57 percent of the variability. Somewhat surprisingly, the relation between exposure to tobacco smoke and the normalized hospital-admission rate was not significant for the boys.

We further compared subgroups of children according to lung function: 21 had relatively normal lung

function, as defined by an FVC of more than 80 percent of the predicted value, and 20 had impaired function (FVC <80 percent of the predicted value). (Vital capacity could not be measured in two children.) Children with poorer lung function had significantly more hospitalizations if there was smoking in the home (8.4 vs. 1.7 admissions; $P = 0.05$). We also compared the children with good nutritional status, as indicated by a weight for height more than 50 percent of the predicted value ($n = 27$), with those with poor nutritional status (weight for height <50 percent of the predicted value; $n = 16$), and there was a trend for more hospitalizations in malnourished children from homes with smokers (6.4 vs. 1.8 admissions for malnourished children from homes without smokers; $P = 0.1$).

Effect of Tobacco Smoke on Pulmonary Symptoms and Function

There was no association between exposure to tobacco smoke, expressed as the number of cigarettes smoked in the home per day, and the amount of coughing or sputum production, the number of nasal polyps, or any pulmonary-function measurement except the percentage of predicted PEFR ($r = -0.39$, $P = 0.01$). The association with PEFR was stronger in the girls ($r = -0.53$, $P = 0.03$) and was also more clearly evident in children with good lung function (95.7 percent for those exposed to tobacco smoke as compared with 118.4 percent for those not exposed; $P = 0.01$). There was also a weak association between the degree of digital clubbing, as measured on a four-point scale (none, mild, moderate, or severe), and the number of cigarettes smoked in the home ($r = 0.30$, $P = 0.05$).

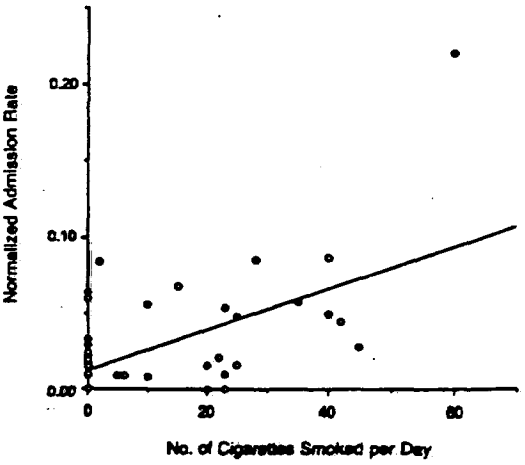

Figure 1. Normalized Admission Rate (Number of Hospital Admissions Divided by the Age of the Child in Months) as a Function of the Number of Cigarettes Smoked in the Home.

The values for the group of 43 children as a whole were $r = 0.58$ and $P<0.0001$; for the 18 girls, $r = 0.76$ and $P = 0.0005$; for the 25 boys, $r = 0.15$ and $P = 0.50$; and for the 24 children from homes with smokers, $r = 0.55$ and $P<0.01$. Girls are represented by solid circles, and boys by open circles.

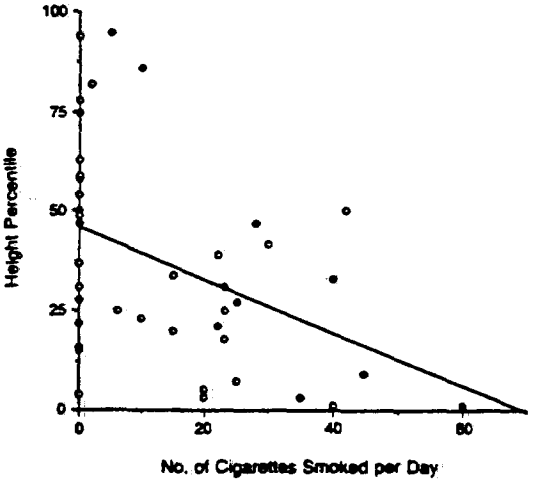

Figure 2. Children's Height Percentiles as a Function of the Number of Cigarettes Smoked in the Home.

The values for the entire group were $r = -0.44$ and $P = 0.003$; for the girls, $r = -0.58$ and $P = 0.01$; for the boys, $r = -0.37$ and $P = 0.07$; and for the group of children from homes with smokers, $r = 0.52$ and $P<0.01$. Girls are represented by solid circles, and boys by open circles.

Effect of Environmental Tobacco Smoke on Growth and Nutrition

Exposure to tobacco smoke was associated most strongly with growth and nutrition (Fig. 2 through 5); a dose-dependent relation was observed for all measurements when the analysis included children not exposed to tobacco smoke (exposure level of 0). The group not exposed to tobacco smoke averaged about the 50th percentile for age for both height and weight. For the girls there was a significant relation ($P<0.05$) between the amount of exposure to tobacco smoke and the height percentile (25 percent of the variability) and weight percentile (33.9 percent of the variability), whereas for the boys there was a trend toward significance correlating exposure to tobacco smoke with the height percentile ($P = 0.067$; 13.8 percent of the variability) but no significant relation with the calculated weight percentile at the start of camp. There was a significant correlation between exposure to tobacco smoke and both the child's height ($r = -0.61$, $P<0.0001$) and the height percentile according to age and sex (Fig. 2). This relation was still valid when only the 24 children from homes with smokers were considered ($r = 0.52$, $P<0.01$). The dose-dependent relation between exposure to tobacco smoke and height was stronger for the girls ($r = -0.82$, $P<0.0001$) than for the boys ($r = -0.42$, $P = 0.03$). A similar correlation was noted between the child's weight and the number of cigarettes smoked in the home for the entire group of children ($r = -0.55$, $P = 0.0002$) and for the girls only

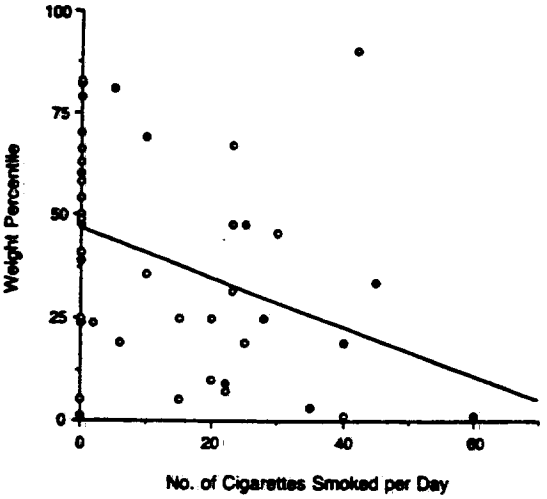

Figure 3. Children's Weight Percentiles as a Function of the Number of Cigarettes Smoked in the Home.

The values for the entire group were $r = -0.37$ and $P = 0.01$; for the girls, $r = -0.50$ and $P = 0.03$; for the boys, $r = -0.12$ and $P = 0.57$; and for the group of children from homes with smokers, $P = 0.36$. Girls are represented by solid circles, and boys by open circles.

($r = -0.77$, $P = 0.0002$), whereas there was a trend toward significance for the boys ($r = -0.33$, $P = 0.11$). There was a dose-dependent inverse correlation between the number of cigarettes smoked by family members each day and the weight percentile according to age and sex (Fig. 3), the midarm circumference (Fig. 4), and triceps skin-fold thickness (Fig. 5), but these correlations failed to achieve significance when data only for the children from homes with smokers were analyzed.

Changes after Two Weeks at Camp

During the two-week camp session significant changes were observed in measures of growth and nutritional status. These included gains in weight, weight percentile, weight-for-height percentile, triceps skin-fold thickness, and midarm circumference. Eight children lost weight over the two weeks of camp, and 29 gained weight. Those who gained weight came from homes where more cigarettes were smoked (mean number of cigarettes smoked daily, 16, as compared with 1.9 cigarettes for those who lost weight; $P<0.02$).

While at camp children from homes with smokers gained more weight than children from smoke-free homes, especially if their initial FVC was normal (Table 1) or weight-for-height percentile was more than the 50th percentile (Table 2).

Discussion

For more than 30 years, nicotine has been known to be a potent regulator of weight in both humans and animals. Tobacco smokers weigh less than nonsmokers[13,14] and gain an average of 5 kg after they stop smoking,[20] half in the first seven weeks.[21] Children exposed to tobacco smoke are smaller and lighter than [redacted].[11] A strong inverse relation between children's height and the number of smokers at home was found for a sample of children in Great Britain, even when growth was adjusted for birth weight, social class, and parental height. This stunting was also unrelated to respiratory symptoms.[8] In a study of children in California, it was shown that exposure to environmental tobacco smoke had a significant ($P<0.001$) inverse and dose-dependent effect on the length at birth and the height at the age of five years that was unrelated to socioeconomic factors.[9] In Canadian children with normal birth weights, those exposed to environmental tobacco smoke were significantly shorter and lighter between the ages of 1 and 6.5 years than those who were not exposed.[11]

Children with cystic fibrosis tend to have low birth weights, and their mean height and weight during childhood are lower than those for the general population.[17,22-24] Although their nutritional requirements are increased, food intake is frequently in the range of 80 percent of the recommended daily allowance of calories and protein for age and height.[22] At all ages, female patients with cystic fibrosis have been reported to have a greater degree of growth suppression and malnutrition than male patients.[24] The mean height percentile was 38 percent for the group of girls we studied and 36 percent for the boys, but the weight-for-height percentile at the start of camp was 47 percent for the girls and 52 percent for the boys, suggesting that although these children were generally smaller than average, they were not particularly thin.

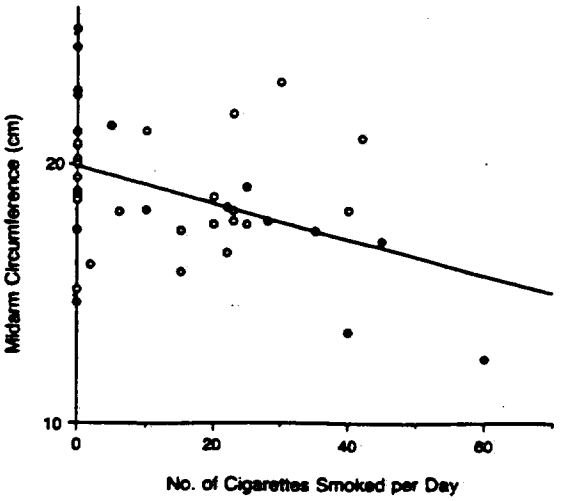

Figure 4. Midarm Circumference as a Function of the Number of Cigarettes Smoked in the Home.

The values for the entire group were $r = -0.42$ and $P = 0.006$; for the girls, $r = -0.68$ and $P = 0.002$; for the boys, $r = -0.17$ and $P = 0.42$; and for the group of children from homes with smokers, $P = 0.10$. Girls are represented by solid circles, and boys by open circles.

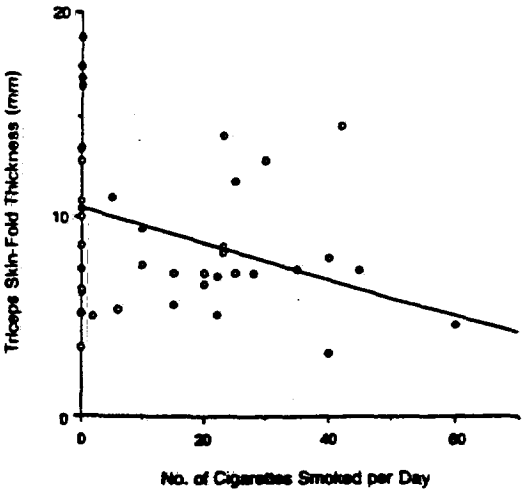

Figure 5. Triceps Skin-Fold Thickness as a Function of the Number of Cigarettes Smoked in the Home.

The values for the entire group were $r = -0.31$ and $P = 0.05$; for the girls, $r = -0.65$ and $P = 0.005$; for the boys, $r = -0.04$ and $P = 0.84$; and for the group of children from homes with smokers, $P = 0.96$. Girls are represented by solid circles, and boys by open circles.

We found that there was a strong dose-dependent association between exposure to environmental tobacco smoke and adverse effects on growth and nutrition, and that these effects were seen most clearly in the girls. Even the children with normal weight-for-height percentiles were often significantly shorter than average, and this was related to the amount of exposure to environmental tobacco smoke in a dose-dependent manner.

In patients with cystic fibrosis who have malabsorption, bicarbonate secretion from the pancreas is less than 10 percent of the normal value, but patients without gastrointestinal symptoms also have a low level of bicarbonate secretion.[25] Studies of conscious dogs given intravenous nicotine equivalent to that in four cigarettes showed a dose-related inhibition of pancreatic and bicarbonate secretions.[26] Although nicotine may act by exacerbating malabsorption, we found no difference between the group with smokers in the home and those without in the degree of malabsorption, as measured by stool consistency or the number of enzyme capsules taken daily.

It has been postulated that the weight-regulating effect of nicotine is due to a lowering of the body weight's set-point.[27] The satiety center in the ventromedial hypothalamus is thought to be under positive serotoninergic control. Pharmacologic treatments that increase serotonin levels or act as agonists at the serotonin receptors decrease food intake.[28] Subacute administration of nicotine increases serotonin in the hypothalamus of rats,[29] and ventilation of cigarette smoke into isolated, perfused rat lungs decreases the rate of serotonin inactivation, which in turn increases the level of circulating serotonin.[30]

Most serotonin is stored in the platelets. Patients with cystic fibrosis tend to have higher mean platelet counts than normal children of the same age regardless of pulmonary status or antibiotic administration.[31] In a study performed 13 years ago at Camp Merrywood, Partington and Ferguson found that the average blood serotonin level in 67 children with cystic fibrosis was twice that in age-matched controls; however, no correlation was found between serotonin levels and height, weight, or skin-fold thickness.[32]

It is possible that there is a relation between lower socioeconomic status, parental smoking, and poor nutrition. Although socioeconomic status was not assessed directly in this study, children exposed to tobacco smoke did not come from larger families than those who were not exposed, nor were there more single-family homes with smokers. Furthermore, in Canada access to health care is not limited by the patient's ability to pay, and health insurance covers nutritional supplements prescribed by a physician. Other studies that have documented an effect of exposure to environmental tobacco smoke on the growth of children have failed to demonstrate a relation with socioeconomic status.[8,9]

It is also possible that exposure to environmental tobacco smoke further increases the energy expenditure of children with cystic fibrosis beyond their capacity to maintain adequate intake for growth[33]; however, the children at camp were generally much more active than they were at home, and yet there was a net gain in weight, midarm circumference, and triceps skin-fold thickness over the two-week session. In all measures of nutrition, the healthiest children from homes with smokers had significantly greater gains than either the children from homes without smokers or the children in poorer health on entry, indicating that some of the effect of tobacco smoke is probably reversible, especially if appropriate weight and lung function can be maintained.

Female patients with cystic fibrosis have poorer nutrition,[34] pulmonary function,[34] and survival[24,35] than male patients at every age. There has been much speculation about the reasons for these differences. Although a much greater effect of exposure to tobacco smoke in girls might partially explain this difference, it is just as likely that both environmental tobacco smoke and some other sex-related factors could operate together to suppress the growth and influence the overall health of the female patients.

There are some limitations to the interpretation of these data. Since the children studied chose to attend camp, there could be unknown factors that made this group of children unrepresentative of the general population with cystic fibrosis, even though the summer camp is available free of charge to all children with cystic fibrosis in Ontario between the ages of 6 and 12 years.

Table 1. Characteristics of Children with Cystic Fibrosis, According to Vital Capacity and Exposure to Environmental Tobacco Smoke.

Forced Vital Capacity*	No. of Children	Values at Start of Camp				Increase during Camp	
		Weight	Weight:Height	Skin-Fold Thickness	Midarm Circumference	Weight	Weight:Height
		kg (percentile)	percentile	mm	cm	kg (percentile)	percentile
≥80% of predicted value							
Exposed to smoke	14	25.7 (35.9)	50.9	8.4	18.7	0.85 (6.6)	9.1
Not exposed	7	32.4 (57.3)	74.3	12.8	21.1	0.013 (0.1)	0
P value		0.01 (0.06)	0.05	0.002	0.01	0.12 (0.05)	0.04
<80% of predicted value							
Exposed to smoke	9	25.3 (26.0)	41.8	7.5	17.6	0.63 (2.7)	5.2
Not exposed	11	30.0 (45.8)	49.5	10.5	19.5	0.40 (2.8)	2.9
P value		0.13 (0.12)	0.56	0.18	0.21	0.47 (0.94)	0.40

*Vital capacity could not be measured in two children.

We made no effort to collect blood or urine samples for measurement of biologic markers of exposure to environmental tobacco smoke; however, there is [illegible] related to a strong, dose-dependent relation between [illegible] and self-reported exposure to tobacco smoke. These levels correlated with the number of smokers in the home and the number of cigarettes smoked at home.[36] More importantly, we did not obtain information about past smoking by the parents or the duration of parental smoking, so it is possible that several of the children listed as coming from smoke-free homes may have had substantial exposure to environmental tobacco smoke. Studies have suggested that the number of cigarettes smoked daily in the home is more strongly related to the child's height than the number of cigarettes smoked during pregnancy or the length of the child at birth.[10]

The absence of an association of pulmonary function with exposure to environmental tobacco smoke in this study could be due to the smallness of the sample; however, the relation between such exposure and pulmonary function in healthy children is open to question[3,4] and is by no means as clear as the relation between exposure to tobacco smoke and growth.

There was also a strong, dose-dependent relation between exposure to tobacco smoke and the normalized hospitalization rate. We did not record the reasons for the hospitalizations, so it is possible that some were not related to cystic fibrosis. What is more interesting is that although nasal polypectomy is one of the most frequent reasons for surgery in children and adults with cystic fibrosis, there is reported to be an association between nasal polyps and good pulmonary function.[37] Although we collected data on the presence or absence of polyps at the time of the initial physical examination at camp, we did not inquire about past polypectomy surgery, nor did we find an association between the presence of nasal polyps and any measurement of nutrition or pulmonary function.

In a recent study of 173 adults with cystic fibrosis, 11 percent regularly smoked tobacco (2 to 60 pack-years), and 20 percent occasionally used marijuana.[38] Although a retrospective comparison with nonsmokers did not show faster short-term pulmonary deterioration in the tobacco smokers, there was no report of the smokers' nutritional status. The very fact that more than half the children we studied were exposed to tobacco smoke at home and that so many adults with cystic fibrosis could choose to smoke suggests that further studies are needed. It is possible that tobacco smoke decreases appetite and growth in children with cystic fibrosis to a greater degree than in the normal population. If these findings are verified by large, population-based studies, then elucidation of the mechanism of this interaction may have far-reaching implications for our understanding of growth in children with cystic fibrosis, sex differences in the clinical course, and the growth-suppressant effects of tobacco smoke in healthy persons.

Table 2. Characteristics of Children with Cystic Fibrosis, According to Weight-for-Height Percentile and Exposure to Environmental Tobacco Smoke.

Weight for Height	No. of Children	Values at Start of Camp				Increase during Camp	
		Weight	Height	Skin-Fold Thickness	Midarm Circumference	Weight	Weight:Height
		kg (percentile)	cm (percentile)	mm	cm	kg (percentile)	percentile
≥50th Percentile							
Exposed to smoke	13	26.3 (37)	125.5 (20.1)	9.3	19.2	0.70 (4.5)	5.4
Not exposed	14	32.6 (58.9)	134.6 (47.7)	13.0	21.1	0.16 (0.1)	0.6
P value		0.004 (0.01)	0.005 (0.003)	0.008	0.03	0.12 (0.03)	0.08
<50th Percentile							
Exposed to smoke	11	24.4 (23.8)	128.7 (42.4)	6.4	17.0	0.80 (5.6)	9.6
Not exposed	5	25.9 (24.2)	132.0 (33.2)	5.6	16.7	0.77 (5.3)	5.8
P value		0.64 (0.98)	0.61 (0.57)	0.49	0.87	0.95 (0.91)	0.47

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